AMENDMENTS TO THE DRAWINGS

The attached Replacement Sheets 9, 10, and 12 of drawings include changes to Figs. 9, 10, and 12 and replaces the original Sheets 9, 10, and 12. The previously omitted sequence identification numbers have been added to Figs. 9, 10, and 12, as follows:

SEQ ID Nos. 1-6 were labeled in Figure 9,

SEQ ID Nos. 7-10 were labeled in Figure 10, and

SEQ ID Nos. 11-20 were labeled in Figure 12.

Attachments: **Replacement Sheet**
Annotated Sheet Showing Changes

REMARKS

This is intended as a full and complete response to the Office Action dated September 25, 2008, having a shortened statutory period for response extended by two months and set to expire on February 25, 2009. Please reconsider the claims pending in the application for reasons discussed below.

In the Office Action, the Examiner considered references previously submitted by the Applicant, but asked additional information for several references. For Citation #13, *Robinson et al.*, the publication date is March 3, 2003. For Citation #5, *Jensen*, the requested publication information is currently unknown to the Applicant. For citation numbers B1 and B3, the related publications U.S. Pub. Nos. 2004-0053875 and 2004-0175703 are listed in the accompanying Supplemental Information Disclosure Statement.

In the specification, the paragraphs [0087] and [0089] have been amended to correctly recite the referenced figure numbers.

In the drawings, the Examiner objected to Figures 9, 10, and 12 for containing sequences not properly labeled with SEQ ID NOs. The Applicant has amended Figures 9, 10, and 12 to illustrate the previously omitted SEQ ID NOs.

Withdrawal of the objection is respectfully requested by the Applicant.

Claims 18, 21-24, 26-28, and 30-38 are pending in the application upon entry of this Response. Claims 19-20 and 25 have been cancelled without prejudice by the Applicant. Claims 30-38 have been added by the Applicant. Claims 18, 21-24, and 26-28 stand rejected by the Examiner. Reconsideration of the rejected claims is requested for reasons presented below.

Claims 18, 21-24, and 26-28 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner asserts that the claims contain subject matter not described in the specification to reasonably convey to the skilled artesian that the inventor had possession of the claimed invention at the time of filing the application. The Applicant respectfully traverses the rejection.

The Examiner asserts that with the exception of the specific vectors disclosed in the specification, the skilled artisan cannot envision the method of claims 26 or 27, particularly wherein the product produced via the method as claims requires at least 100 or 1,000 heterogeneous siRNAs. The Examiner states that *Li* (*Li et al.*, as cited in the OA) teaches that the efficiency of siRNA is dependent on the siRNA sequence, the secondary structures of siRNA and mRNA, and that off-target effects can prevent the use of siRNA as treatments. (OA, page 4-6). The Applicant respectfully disagrees with the Examiner.

The Applicant asserts that the claimed subject matter is described in the specification to reasonably convey to the skilled artesian that the inventor had possession of the claimed invention at the time of filing the application. Embodiments of the present invention actually address the problems articulated by the Examiner and *Li*. It is certainly true that not all possible siRNA sequences imaginable would efficiently affect gene expression--that is, not all siRNA sequences are "effector sequences" in the lexicon of the application. Embodiments of the present invention provide methods for screening the efficiency and efficacy of siRNA sequences, from 100s to 1000s or more at a time.

For example, Figure 1 directly addresses this problem. Figure 1 shows a process where first, an effector library is constructed (a library is constructed of putative siRNA sequences); second, target cells are transduced with the effector library; third, a desired cell phenotype is selected (that is, a cell with a desired phenotype caused by a particular putative siRNA is selected); and last, the sequence of the siRNA that caused the desired phenotype is identified (see also paragraph 33 wherein Figure 1 is described). In addition, Figures 2, 4, and 5 illustrate this screening or selection process--and paragraphs 34, 61, and 62 describe this screening or selection process--in more detail. Because the invention actually solves the problem that the Examiner has identified, the Applicant hereby respectively asserts that the rejection of claims 18, 21-24, and 26-28 under 35 U.S.C. § 112, first paragraph, is not appropriate and should be withdrawn.

Withdrawal of the rejection is respectfully requested by the Applicant.

Claims 18, 21-24, and 26-28 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over *Beraud et al.*, WO 2004/108897, herein *Beraud* and *Adessi et al.*, Solid Phase DNA Amplification: Characterization of Primer Attachment and Amplification Mechanisms, Nucleic Acids Research, (2000) 28 (20): e87, 8 pages, herein *Adessi*. The Examiner asserts it would have been obvious for the skilled artesian to substitute the bead based solid phase synthesis or bead as disclosed by *Beraud* for another microarray synthesis or glass slide as disclosed by *Adessi*. The Applicant respectfully traverses the rejection in view of the amended claims.

Therefore, *Adessi*, alone, does not teach, show, or suggest a method for making a packaged viral effector library, comprising cloning a defined set of nucleic acid sequences into viral expression vectors to produce a library of effector constructs, wherein the defined set of nucleic acid sequences comprises at least 100 different effector sequences and is made by a process comprising synthesizing a set of nucleic acid sequences on a surface of a microarray, wherein each nucleic acid sequence has a specific sequence, has a length of at least 70 nucleotides, and is synthesized in a specific location of the surface, detaching the set of nucleic acid sequences from the microarray, and amplifying the detached set of nucleic acid sequences by polymerase chain reaction, thereby generating the defined set of nucleic acid sequences, and packaging the library of effector constructs into viral particles to produce a viral effector library, as recited in claim 26, and claims 18 and 21-24 dependent thereon.

Also, *Adessi*, alone, does not teach, show, or suggest a method for making a library of effector constructs, comprising synthesizing a set of at least 100 different effector nucleic acid sequences on a surface of a microarray, wherein each nucleic acid sequence has a specific sequence, has a length of at least 70 nucleotides, and is synthesized in a specific location of the surface, detaching the set of nucleic acid sequences from the microarray, amplifying the detached set of nucleic acid sequences by polymerase chain reaction, thereby generating a defined set of nucleic acid sequences, and cloning the defined set of nucleic acid sequences into viral expression vectors to produce a library of effector constructs, as recited in claim 27, and claim 28 dependent thereon.

Withdrawal of the rejection is respectfully requested by the Applicant.

Claims 18, 21-24, and 26-28 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over *Caplan et al.*, U.S. Pub. No. 2003/0149113, herein *Caplan*, in view of *Fosnaugh et al.*, U.S. Pub. No. 2003/0148507, in view of *Barone et al.* U.S. Pat. No. 7,026,114, herein *Barone*. The Examiner asserts it would have been obvious for the skilled artesian to substitute the bead based solid phase synthesis or bead as disclosed by *Caplan* or *Fosnaugh* for another microarray synthesis or glass slide as disclosed by *Barone*. The Examiner further asserts that the siRNA library of a specific size as taught by *Fosnaugh* would have yielded predictable results. The Applicant respectfully traverses the rejection in view of the amended claims.

Therefore, *Caplan*, *Fosnaugh*, and *Barone*, alone or in combination, do not teach, show, or suggest a method for making a packaged viral effector library, comprising cloning a defined set of nucleic acid sequences into viral expression vectors to produce a library of effector constructs, wherein the defined set of nucleic acid sequences comprises at least 100 different effector sequences and is made by a process comprising synthesizing a set of nucleic acid sequences on a surface of a microarray, wherein each nucleic acid sequence has a specific sequence, has a length of at least 70 nucleotides, and is synthesized in a specific location of the surface, detaching the set of nucleic acid sequences from the microarray, and amplifying the detached set of nucleic acid sequences by polymerase chain reaction, thereby generating the defined set of nucleic acid sequences, and packaging the library of effector constructs into viral particles to produce a viral effector library, as recited in claim 26, and claims 18 and 21-24 dependent thereon.

Also, *Caplan*, *Fosnaugh*, and *Barone*, alone or in combination, do not teach, show, or suggest a method for making a library of effector constructs, comprising synthesizing a set of at least 100 different effector nucleic acid sequences on a surface of a microarray, wherein each nucleic acid sequence has a specific sequence, has a length of at least 70 nucleotides, and is synthesized in a specific location of the surface, detaching the set of nucleic acid sequences from the microarray, amplifying the detached set of nucleic acid sequences by polymerase chain reaction, thereby generating a defined set of nucleic acid sequences, and cloning the defined set of

nucleic acid sequences into viral expression vectors to produce a library of effector constructs, as recited in claim 27, and claim 28 dependent thereon.

Withdrawal of the rejection is respectfully requested by the Applicant.

In conclusion, the references cited by the Examiner, alone or in combination, do not teach, show, or suggest the claimed invention.

Having addressed all issues set out in the Office Action, the Applicant respectfully submits that the claims are in condition for allowance and respectfully request that the claims be allowed.

Respectfully submitted,

John-Paul F. Cherry
Registration No. 57,323
PATTERSON & SHERIDAN, L.L.P.
3040 Post Oak Blvd., Suite 1500
Houston, TX 77056
Telephone: (713) 623-4844
Facsimile: (713) 623-4846
Agent for the Applicant